CLAIMS

1. A process of purifying citalopram, either in racemic or enantiomeric form, which process comprises:

(i) providing a crude mixture comprising citalopram, either in racemic or enantiomeric form, dissolved in a water immiscible organic solvent, and which mixture also includes one or more citalopram derivatives which are present as citalopram impurities;

(ii) washing said crude mixture with at least one dilute aqueous solution of a polybasic acid, either in free form or as a partial alkali metal salt, so as to separate said citalopram from citalopram impurities present in said crude mixture; and

(iii) where required converting citalopram free base, separated from citalopram impurities further to step (ii), to a pharmaceutically acceptable salt.

2. A process according to claim 1, which comprises carrying out an initial washing of the crude mixture with at least one dilute aqueous solution of a polybasic acid, either in free form or as a partial alkali metal salt, so as to remove citalopram impurities from the crude mixture, and subsequently washing the residual crude mixture with at least one further dilute aqueous solution of a polybasic acid, either in free form or as a partial alkali metal salt, so as to separate citalopram, either in racemic or enantiomeric form, from the impurities remaining in the crude mixture, by extraction of citalopram, as a salt formed with the polybasic acid, into an aqueous phase.

3. A process according to claim 2, wherein the impurities removed from the crude mixture by the initial washing with said at least one dilute aqueous solution of a polybasic acid have a basicity of greater than the basicity of citalopram.

4. A process according to claim 3, wherein the impurities remaining in the crude mixture further to the initial washing with said at least one dilute aqueous solution of said polybasic acid have a basicity of less than the basicity of citalopram.

5. A process according to any of claims 2 to 4, wherein a base is added to the aqueous phase containing citalopram as a salt of the polybasic acid, in an amount sufficient to liberate citalopram free base which is then extracted into an organic solvent.

6. A process of purifying citalopram, either in racemic or enantiomeric form, which process comprises:

(i) providing a crude mixture comprising citalopram, either in racemic or enantiomeric form, dissolved in a water immiscible organic solvent, and which mixture also includes one or more citalopram derivatives which are present as citalopram impurities;

(ii) washing said crude mixture with at least one dilute aqueous solution of a polybasic acid, either in free form or as a partial alkali metal salt, so as to remove citalopram impurities from the crude mixture;

(iii) washing the residual crude mixture obtained further to step (ii) with at least one further dilute aqueous solution of a polybasic acid, either in free form or as a partial alkali metal salt, so as to separate said citalopram from impurities remaining in said residual crude mixture, by extraction of citalopram, as a salt formed with the polybasic acid, into an aqueous phase and optionally washing the resulting aqueous phase with an organic solvent;

(iv) adding a base to the aqueous phase in an amount sufficient to liberate citalopram free base and extracting the liberated citalopram into an organic solvent;

(v) optionally re-extracting citalopram free base from the organic extract obtained further to step (iv) by washing with at least one further dilute aqueous solution of a polybasic acid, either in free form or as a partial alkali metal salt, so as to extract citalopram, as a salt formed with the polybasic acid, into an aqueous phase and adding thereto a base in an

amount sufficient to liberate citalopram free base and further extracting the liberated citalopram into an organic solvent; and

(vi) where required converting the free base obtained further to step (iv) or (v) to a pharmaceutically acceptable salt thereof.

7. A process according to claim 1 to 6, wherein the water immiscible solvent employed in step (i) is selected from the group consisting of toluene, ethyl acetate, hexane and methylene dichloride.

8. A process according to claim 7, wherein the water immiscible solvent is toluene or ethyl acetate.

9. A process according to any of claims 1 to 8, wherein the polybasic acid is selected from the group consisting of tartaric acid, oxalic acid, fumaric acid, citric acid and edetic acid, which can either be employed in free form, or as a partial alkali metal salt.

10. A process according to claim 9, wherein the alkali metal salt is the sodium salt.

11. A process according to claim 9, wherein the polybasic acid is edetic acid.

12. A process according to claim 11, wherein said edetic acid is employed as disodium edetate.

13. A process according to any of claims 6 to 12, wherein the initial washing of the crude mixture with said at least one dilute aqueous solution of said polybasic acid of step (ii) removes impurities from the crude mixture having higher basicity compared to citalopram.

14. A process according to claim 3 or 13, wherein the initial washing removes one or more of the following impurities if present in the crude mixture: 5- carboxamide citalopram, N-desmethyl citalopram, desfluoro citalopram, 4[4-(dimethylamino)-1-(4'-

fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)-benzonitrile and / or 5-formyl citalopram.

15. A process according to any of claims 2 to 14, wherein the strength of the dilute aqueous solution of said polybasic acid employed in the initial washing is in the range of 0.5% to 6%.

16. A process according to any of claims 2 to 15, wherein the subsequent washing separates citalopram from the residual crude mixture, whereby citalopram as a salt formed with disodium edetate is extracted into an aqueous phase.

17. A process according to any of claims 6 to 16, wherein the impurities remaining in the residual crude mixture subsequent to the initial washing have a basicity of less than citalopram.

18. A process according to claim 4 or 17, wherein the impurities remaining in the residual crude mixture subsequent to the initial washing are selected from the group consisting of descyano citalopram, 5-chloro citalopram and 5-bromo citalopram.

19. A process according to any of claims 2 to 18, wherein the strength of the dilute aqueous solution of a polybasic acid, either in free form, or as a partial alkali metal salt, as employed in the subsequent washing stage is in the range of 4% to 25%.

20. A process according to any of claims 2 to 19, wherein the subsequent washing is carried out at a temperature in the range of 40 to 80°C.

21. A process according to any of claims 5 to 20, wherein said base comprises an aqueous alkali metal hydroxide solution.

22. A process according to claim 21, wherein the base is aqueous sodium hydroxide or potassium hydroxide.

23. A process according to any of claims 5 to 22, wherein the liberated citalopram free base is extracted from the aqueous phase into ethyl acetate.

24. A process according to any of claims 1 to 23, which includes converting citalopram free base to a pharmaceutically acceptable salt of citalopram.

25. A process according to claim 24, wherein the pharmaceutically acceptable salt is selected from the group consisting of the hydrobromide, hydrochloride and oxalate.

26. A process of preparing citalopram, either in racemic or enantiomeric form, by ring closure of 4-[4-(dimethylamino)-1-(4'-fluorophenyl)-1-hydroxybutyl]-3(hydroxymethyl)-benzonitrile, dissolving the resulting citalopram, together with one or more citalopram derivatives which are present as citalopram impurities, in a water immiscible organic solvent so as to provide a crude mixture thereof, and subjecting the resulting crude mixture to a purification process according to any of claims 1 to 25.

27. A process of preparing citalopram, either in racemic or enantiomeric form, by conversion of 1-[3-(dimethylamino)propyl]-1-(4-flurophenyl)-5-bromo pthalane to the corresponding cyano derivative, namely citalopram, dissolving the resulting citalopram, together with one or more citalopram derivatives which are present as citalopram impurities, in a water immiscible organic solvent so as to provide a crude mixture thereof, and subjecting the resulting crude mixture to a purification process according to any of claims 1 to 25.

28. Use of at least one polybasic acid, either in free form or as a partial alkali metal salt, in the purification of citalopram, either in racemic or enantiomeric form.

29. Use (i) of at least one polybasic acid, either in free form or as a partial alkali metal salt, so as to remove one or more citalopram impurities from a crude mixture including citalopram, either in racemic or enantiomeric form, wherein said citalopram impurities comprise one or more citalopram derivatives having higher basicity compared to citalopram; in combination with use (ii) of at least one polybasic acid, either in free form or

as a partial alkali metal salt, so as to separate citalopram, either in racemic or enantiomeric form, from the impurities remaining in the residual crude mixture obtained further to use (i), by extraction of citalopram, as a salt formed with the polybasic acid, into an aqueous phase.

30. Use according to claim 28 or 29, wherein the polybasic acid is selected from the group consisting of tartaric acid, oxalic acid, fumaric acid, citric acid and edetic acid, which can either be employed in free form, or as a partial alkali metal salt.

31. Use according to claim 30, wherein the alkali metal salt is the sodium salt.

32. Use according to claim 30, wherein the polybasic acid is edetic acid.

33. Use according to claim 32, wherein said edetic acid is employed as disodium edetate.

34. Citalopram free base, or a pharmaceutically acceptable salt thereof, either in racemic or enantiomeric form, prepared by a process according to any of claims 1 to 27.

35. Citalopram according to claim 34, which includes less than about 0.1% citalopram derivatives present as citalopram impurities.

36. Citalopram according to claim 35, which is more than 99.7% w/w pure (peak area).

37. A pharmaceutical formulation comprising citalopram according to any of claims 34 to 36, together with a pharmaceutically acceptable carrier or excipient therefor.

38. Citalopram according to any of claims 34 to 36, for use in the manufacture of a medicament for the treatment of a disease state prevented, ameliorated or eliminated by the administration of a serotonin reuptake inhibitor.

39. A method of treating a disease state prevented, ameliorated or eliminated by the administration of a serotonin reuptake inhibitor in a patient in need of such treatment, which method comprises administering to the patient an effective amount of citalopram according to any of claims 34 to 36.

40. A process of purifying citalopram, either in racemic or enantiomeric form, substantially as illustrated by the Examples.

41. A process of preparing citalopram, or a pharmaceutically acceptable salt thereof, either in racemic or enantiomeric form, substantially as illustrated by the Examples.

42. Citalopram prepared substantially as described in the Examples.